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Green chemistry: A powerful approach to pollution prevention, waste minimization and hazard reduction

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Introduction

Historically, the best practices for chemical use in the laboratory have focused on safe handling (including the proper use of environmental controls and personal protective gear) and proper waste treatment and/or disposal. Although these practices are well-established and, when properly implemented, protect laboratory workers from exposure to hazardous materials, the strategy has limitations. Methods used to limit exposure (e.g. fume hoods) are expensive, can fail to protect the worker due to mechanical failure or improper use and transport contaminants into the environment. Waste treatment and disposal is expensive, hazardous, can lead to exposure and environmental contamination and does nothing to minimize the consumption of non-renewable resources. Thus, it is important to consider whether new strategies that go beyond personal protection and proper waste disposal can be effectively implemented to reduce laboratory hazards and waste generation.

In this paper I describe a new approach to hazard reduction and pollution prevention, so-called “green” chemistry. Green chemistry is a fundamentally different approach to improving laboratory health and safety because it focuses on the reduction of the intrinsic hazards of the materials used in the laboratory and on the minimization of waste generated. In the following sections, I will first define green chemistry and describe its relationship to other risk reduction and waste minimization approaches. Next, I will explain the principles and strategies used to implement green chemistry, followed by some examples of green chemistry applications. Finally, I will suggest some opportunities to implement green chemistry in academic teaching and research laboratories and suggest some resources for obtaining more information about implementing green chemistry.

Important terms related to green chemistry

There are a number of important concepts and terms related to green chemistry. Here, each of these is listed and the some the key relationships between the terms are explained.

Waste minimization – any practice that reduces or eliminates the generation of waste, including reduction or elimination of material use, recycling or reuse. A common example of waste minimization in an academic setting is the use of microscale laboratory glassware.

Pollution prevention – this concept was formalized in the *Pollution Prevention Act of 1990*. The following is an excerpt from the EPA’s website at:

<http://www.epa.gov/p2/p2policy/definitions.htm#sourc>

“Pollution prevention means “source reduction,” as defined under the Pollution Prevention Act, and other practices that reduce or eliminate the creation of pollutants through:

- increased efficiency in the use of raw materials, energy, water, or other resources, or
- protection of natural resources by conservation.

The Pollution Prevention Act defines "source reduction" to mean any practice which:

- reduces the amount of any hazardous substance, pollutant, or contaminant entering any waste stream or otherwise released into the environment (including fugitive emissions) prior to recycling, treatment, or disposal; and
- reduces the hazards to public health and the environment associated with the release of such substances, pollutants, or contaminants.

The term includes: equipment or technology modifications, process or procedure modifications, reformulation or redesign of products, substitution of raw materials, and improvements in housekeeping, maintenance, training, or inventory control."

Hazard reduction – practices that reduce the risk associated with chemical exposure through approaches that minimize the inherent hazard of the material. The *risk* can be described as a function of both the hazard of the material and the exposure to it (Eq. 1). Hazard reduction differs from approaches that focus on minimizing exposure (through environmental controls and personal protective gear) because it minimizes the inherent hazard. Based upon the relationship between risk, hazard and exposure, if the hazard is minimized, so is the risk. If, on the other hand, one attempts to prevent exposure, the risk will be maximum if environmental controls are improperly used or fail.

$$\text{risk} = f [\text{hazard, exposure}] \quad (1)$$

Whereas the strategies of waste minimization and source reduction focus on the quantity of waste generated, hazard reduction methods emphasize the reduction of the inherent hazard associated with the material used.

What is "green" chemistry?

Defn: Green chemistry is the utilization of a set of principles that reduces or eliminates the use or generation of hazardous substances in the design, manufacture and application of chemical products.¹

The green chemistry approach addresses both hazard reduction and waste minimization. It relies on the molecular-level design of chemical products that have reduced hazard and of chemical transformations and applications that minimize the generation of waste and reduce the impact on the environment. The emphasis is on eliminating hazard rather than just preventing exposure. Hazard is acknowledged as another important property of matter. Green chemistry (as known as clean technology, environmentally-benign chemistry or benign by design) involves inventing new methods to reduce chemical hazards while producing superior products in a more efficient (and economical) fashion. In addition, green chemistry approaches embrace chemistry as the solution rather than the problem.

Some well-known examples of green chemistry are the removal of lead from paint and gasoline or the use of environmentally-benign carbon dioxide (in its supercritical form) to extract caffeine from coffee. At the most fundamental level, the strategies of green chemistry involve: preventing the formation of waste in the first place, employing more benign reagents or solvents

¹ Anastas, P. T.; Warner, J. C. *Green Chemistry: Theory and Practice*, Oxford University Press, 1998. pp 135.

and implementing selective and efficient transformations. The principles of green chemistry and specific examples of how it can be implemented in the academic laboratory will be detailed in subsequent sections of this paper.

What are the potential benefits of adopting green chemistry in an academic lab setting?

Any change in the way that we approach our work in the lab requires an investment of time, energy and money. Thus, it is important to consider the benefits of adopting green chemistry approaches to determine whether there will be a satisfying return on investment. We have found a number of important benefits in our program. The practical benefits include the fact that the costs for waste disposal have been reduced, the working environment is safer, and there are fewer accidents. In addition, the change provided an opportunity to modernize our curriculum, recruit new undergraduate and graduate students to campus using green chemistry as a competitive advantage and generally improve the educational and research environment (students typically perform better in a safer environment). The program has also brought the university excellent national and international press and been a focus for fundraising efforts. Green chemistry provides many immediate and long-term benefits. The challenge involves finding those that make such a program most beneficial in each college or university setting.

Green chemistry principles, strategies and tools

A good starting point for identifying opportunities for waste prevention and hazard reduction is to consult the *12 Principles of Green Chemistry* put forward by Anastas and Warner. The principles provide some suggestions for focusing one's efforts developing new or improving existing products or processes. The principles are listed, and briefly summarized, below. For more information on the principles, please consult the original text.¹

1. *It is better to **prevent waste** than to treat or clean up waste after it is formed.* The key here is to change the mindset to planning for **waste prevention** rather than anticipating waste management and treatment.
2. *Synthetic methods should be designed to **maximize the incorporation of all materials used in the process into the final product.*** Consider atom economy and materials efficiency in the choice or design of synthetic transformations. Choosing transformations that incorporate most of the starting materials into the product is more efficient and minimizes waste.
3. *Wherever practicable, synthetic methodologies should be designed to **use and generate substances that possess little or no toxicity to human health and the environment.*** The goal is to use **less hazardous reagents** whenever possible and design processes that do not produce hazardous by-products. Often a range of reagent choices exist for a particular transformation – choose the reagents that pose the least risk and generate only benign by-products.
4. *Chemical products should be designed to **preserve efficacy of function while reducing toxicity.*** Toxicity and ecotoxicity are properties of the product. New products can be designed that are inherently safer, while highly effective for the target application. In academic labs this principle should influence the design of synthetic targets and new products.
5. *The use of **auxiliary substances (e.g. solvents, separation agents, etc.) should be made unnecessary whenever possible and, innocuous when used.*** Solvent use leads to considerable waste. Reduction of solvent volume or complete elimination of the solvent is

often possible. In cases where the solvent is needed, less hazardous replacements should be employed. Purification steps also generate large sums of solvent and other waste (chromatography supports, e.g.). Avoid purifications when possible and minimize the use of auxiliary substances when they are needed.

6. **Energy requirements** should be recognized for their environmental and economic impacts and **should be minimized**. Synthetic and purification methods should be conducted so that heating and cooling is minimized.
7. A raw material **feedstock should be renewable** rather than depleting whenever technically and economically practicable. In academic labs, this may be more of a research problem than a readily implemented in-lab solution.
8. Unnecessary **derivatization** (blocking group, protection/deprotection, temporary modification of physical/chemical processes) **should be avoided** whenever possible. Synthetic transformations that are more selective will eliminate or reduce the need for protecting groups. In addition, alternative synthetic sequences may eliminate the need to transform functional groups in the presence of other sensitive functionality.
9. **Catalytic reagents** (as selective as possible) are superior to stoichiometric reagents. Catalysts can serve several roles during a transformation. They can enhance the selectivity of a reaction, reduce the temperature of a transformation, enhance the extent of conversion to products and reduce reagent-based waste (since they are not consumed during the reaction). By reducing the temperature, one can save energy and potentially avoid unwanted side reactions.
10. **Chemical products should be designed so that at the end of their function they do not persist in the environment and break down into innocuous degradation products**. Again, this is more of a research topic, this time relating to how molecular-level design can be used to design products that will degrade into harmless substances when they are released into the environment.
11. Analytical methodologies need to be further developed to allow for **real-time in-process monitoring and control** prior to the formation of hazardous substances. It is always important to monitor the progress of a reaction to know when the reaction is complete or to detect the emergence of any unwanted by-products. Either in situ or ex situ monitoring will suffice in the academic lab.
12. Substances and the form of a substance used in a chemical process should be chosen so as to **minimize the potential for chemical accidents, including releases, explosions, and fires**. Choosing reagents and solvents that minimize the potential for chemical accidents, including releases, explosions, and fires is always good practice in any laboratory setting.

Implementation of waste minimization and green chemistry strategies in academic teaching and research labs. There are numerous opportunities to reduce hazards and minimize waste in our laboratories. First I will address the waste minimization strategies that can be implemented, followed by the green chemistry approach. As you will see, the latter approach offers larger potential gains and, in many cases, is more consistent with our teaching and research goals.

Waste minimization strategies that have been implemented in the academic lab often include:

- Conducting chemical transformations at reduced scale – for example the use of microscale glassware.
- Reducing the amounts of solvents used in cleaning glassware

- Having students work in teams as opposed to as individuals
- Performing simulated/virtual experiments using computer programs in place of wet chemistry work

Each of these approaches can be effectively used to reduce waste, but, in some cases, may sacrifice other goals. For example, use of virtual experiments and team-based experiments will decrease the amount of hands-on laboratory experience the students get. Conducting microscale experiments reduces waste, but does not address the hazards of the materials used and will not suffice if larger amounts of material need to be prepared.

Green chemistry can be readily implemented in teaching and research labs in order to reduce hazards and minimize waste. Through the remainder of this section, I will describe some examples of how green chemistry has been implemented in a sophomore-level organic chemistry laboratory course at the University of Oregon. The strategies described here easily transfer to the research laboratory.

The first step in implementing green chemistry is identifying the opportunities where green chemistry can effectively be incorporated. This can be done by an application of the 12 Principles of Green Chemistry (described above) or using a visual approach that we developed for our Green Organic Chemistry Laboratory course. [2] We start by writing down an equation for the chemical transformation to be performed (analogous to the generic transformation illustrated below). We then analyze the transformation by:



- **Assessing** the reaction conditions and products
- **Identifying** hazardous materials or inefficient procedures
- **Modifying** the process/product and testing efficacy of the modification

Three of the most easily addressed areas that can be addressed to minimize waste and hazards through green chemistry include: solvents, reagents and reaction efficiency. Examples of each of these areas are given below. In each case, I describe some specific examples taken from the Green Organic Laboratory curriculum developed at the University of Oregon. A graphical Table of Contents for the text² describing this curriculum is provided in Appendix 1. References in the text to *Experiment #X* can be found in the appendix.

Reduce or eliminate solvent use

² Doxsee, K. M.; Hutchison, J. E. *Green Organic Chemistry: Strategies, Tools and Laboratory Experiments*, First Edition, Brooks/Cole, 2004. pp. 244. Contains ten chapters of background on green chemistry and 19 original laboratory experiments.

Nearly all of the waste volume in an academic lab is typically solvent waste, so there is considerable opportunity for reducing the volume of the wastestream by focusing on the reduction of elimination of solvents used. We traditionally use solvents to clean glassware, in purification steps and as medium in which to conduct reactions. In each of these situations, there are opportunities to reduce solvent use.

Reducing solvent use in glassware cleaning and chemical purification steps can often be accomplished through increasing awareness that solvent use can be reduced and some simple practical steps. Instead of relying on solvents to remove *all* residue from glassware, we can use a small amount of solvent to remove gross chemical contamination and make greater use of detergents for thorough glassware cleaning. In addition, it is often possible to recycle the solvents we use for the initial removal of chemicals from the glassware. In the case of purifications, the use of recrystallization as opposed chromatography often reduces the volume of solvent used. By selecting more efficient reaction pathways that lead to high conversions, purification steps can be eliminated or reduced, leading to solvent use reduction.

One can also minimize or, in some cases, eliminate the use of the solvent as the medium for synthetic transformations. We often use more solvents than we need to carry out the synthesis. It is useful to consider whether the transformation might be carried out safely and efficiently using less solvent. In the case of higher boiling solvents, it is often more convenient to use less solvent because this facilitates isolation and purification of the product.

Although it is typically assumed that a solvent is necessary to effect reaction between reactants, a growing number of examples illustrate that reactions can be effectively carried out in the absence of solvent. Two approaches are common, including gas-phase reactions and the reaction between solids. We have incorporated both of these approaches in our undergraduate curriculum. In *Experiment 17*, an aldol condensation can be effectively carried out between two solids because the two reactants form a eutectic mixture that melts at room temperature and permits mixing of the two reactants without the need for a solvent. In another example, pyrrole and benzaldehyde react in the gas-phase to produce tetraphenylporphyrin (*Experiment 6*). The absence of solvent in the latter case greatly simplifies purification relative to traditional solvent-based preparations. These two examples illustrate some of the additional benefits associated with solventless reactions.

Alternative solvents

In some cases, it isn't possible to reduce or eliminate the solvent without adversely impacting the specificity or efficiency of the reaction. In those cases, one can often reduce waste and hazard in a chemical transformation by using an alternative solvent. In choosing a replacement solvent, one should consider at least the health effects of exposure (toxicity, e.g.) and the potential for environmental impact. With respect to these criteria, the use of alcohols, water, esters, (some) ketones and aliphatic hydrocarbons is typically preferred instead of aromatic and chlorinated solvents. Of course, one must keep in mind a number of practical issues associated with solvent choice. The alternative solvents must be capable of dissolving the reactants, should have an appropriate liquid range, and facilitate the reaction and separation.

In our teaching lab the use of alternative solvents is a common strategy that can be easily implemented in a wide variety of cases. The substitution of toluene for benzene and methylene chloride for chloroform or carbon tetrachloride are examples that have been widely applied to reduce hazards associated with benzene and carbon tetrachloride. However, there are many more opportunities for more substitutions that can eliminate the use of aromatic or chlorinated solvents. For example, we have conducted bromination reactions in ethanol instead of chlorinated solvents (*Experiments 1 and 2*), Diels-Alder reactions in water instead of toluene, and C-C bond forming reactions (*Experiment 12*) in aqueous alcohols rather than in chlorinated solvents. In each case, the transformations are efficient in the new reaction medium and can be carried out under mild reaction conditions that lead to crude products that are easy to purify. In some cases, such as the Diels-Alder reaction, the solvent switch *improves* the reaction efficiency by accelerating the reaction. Another recent example of the benefits of solvent substitution involves the use of liquid carbon dioxide as a solvent for the extraction of natural products (e.g. limonene from orange peel).³

Greener reagents

Another approach to greening a reaction is to consider the reagents used. Whereas the solvent often contributes the most volume to the wastestream, reagents (and their by-products) are often responsible for the hazard of the workplace and the wastestream. It is frequently the case that the reagents used during a transformation are considerably more reactive than necessary and this reactivity often leads to increased hazard. Thus, an approach to reducing hazard is to choose reagents that are just reactive enough to effect the transformation. This strategy provides an additional, but important, practical benefit – when reactivity is reduced, selectivity increases, thereby reducing by-products.

In the academic lab, the use of more benign reagents enhances lab safety, in addition to reducing the hazard of the wastestream. For example, in *Experiment 4*, we have substituted hydrogen peroxide (plus a catalyst) in place of nitric acid in the synthesis of adipic acid⁴ and have made use of a solid brominating agent (pyridinium tribromide) or HBr/hydrogen peroxide (in *Experiments 1 and 2*, respectively) in place of liquid bromine. In each of these cases, the lab environment is made safer. Given the wide range of reagents available to effect organic and inorganic transformations, instructors and researchers now have many options to choose from, and have an opportunity to choose reagents that are greener.

Catalytic reagents

Even in the case of excellent reagent choice, a stoichiometric reagent is consumed in the reaction, thus catalytic reagents will provide opportunities to enhance the materials efficiency of the transformation. Catalysis is a powerful approach to greening a reaction in that many of the principles of green chemistry can be addressed by using a catalytic reagent. The amount of reagent needed is reduced, the energy needed to carry out the transformation is reduced, the

³ McKenzie, L. C.; Thompson, J. E.; Sullivan, R.; Hutchison, J. E. "Green chemical processing in the teaching laboratory: A convenient liquid CO₂ extraction of natural products," *Green Chem.* **2004**, 355-358.

⁴ Reed, S. M.; Hutchison, J. E. "Green Chemistry in the Organic Teaching Laboratory: An Environmentally Benign Synthesis of Adipic Acid," *J. Chem. Educ.* **1999**, 77, 1627-1629.

degree of conversion of raw materials to product is often higher, the selectivity may be higher and it is possible to design catalysts with desired reactivity and selectivity.

Instructors and researchers should keep an eye out for new catalytic reactions that can be applied in the teaching or research labs. A number of catalytic reactions can be done in the teaching lab, including transition metal mediated coupling reactions to form C-C bonds (see *Experiments 5* and *12*) and catalytic oxidation (*Experiment 4*)⁴ or reduction reactions. Given the wide range of advantages that catalysts offer, this should be an area of focus for further development in research and the teaching laboratories.

Atom economy

For most functional group transformations and more complex syntheses, there are now a wide range of choices of solvents, reagents and reaction conditions. We have already discussed some of the green chemistry options related to solvents and reagent choice, specifically related to the hazards associated with their use. We should also consider the efficiency of material use when choosing a reagent or a synthetic pathway. *Atom economy* is a concept that provides us a means of assessing the percentage of atoms used as reactants (starting material and reagents) that become incorporated into the product. In general *addition* reactions (e.g. a Diels-Alder reaction) have high atom economy because all of the atoms contained in the reactants are found in the product. On the other hand, elimination reactions or those involving complex reagents that don't get incorporated into the product have poor atom economy. We should strive for reactions that have high atom economy because this inherently minimizes waste (both in the immediate reaction and in synthesis of the reactants).

We have incorporated several experiments in our teaching labs that illustrate atom economy. In one case (*Experiment 1*), the use of pyridinium tribromide (in place of bromine), although safer is shown to have poorer atom economy. For every alkene that is brominated, one equivalent of pyridinium hydrobromide is produced. An alternative procedure (*Experiment 2*) for bromination (HBr/H₂O₂) is used as an approach that has a higher atom economy.⁵ The Diels-Alder experiment described earlier is a good example of a reaction that has a high atom economy (100%).

Putting waste to work

A final example of a green chemistry approach that primarily applies to the teaching labs involves using a product from one reaction as the starting material for another. In the research lab this is common practice because most transformations are multiple step syntheses. However, in the teaching lab, the students will often make large quantities of the desired product that must then be treated as waste. It is therefore useful to carefully choose transformations that teach the reaction chemistry and lab skills that one desires to teach and produces a product that is useful as the starting material for another laboratory exercise. One example from our curriculum is the production of cyclohexene during *Experiment 3* (this teaches the synthesis of alkenes and distillation) that is used in *Experiment 4* for the synthesis of adipic acid.⁴ It may also be possible

⁵ McKenzie, L. C.; Huffman, L. M.; Hutchison, J. E. "The Evolution of a Green Chemistry Laboratory Experiment: Greener Brominations of Stilbene," *J. Chem. Educ.* **2004**, *In press*.

to use the material produced in one course as the starting material needed in a different course or in a research project.

Summary

Green chemistry provides a number of opportunities to make our labs safer and reduce the volume and toxicity of the waste that we generate. In addition, it offers a number of opportunities to dramatically improve our chemistry by making it more convenient or more efficient. Green chemistry provides competitive advantage in that it can be economically more profitable or may provide concrete recruiting advantages. If you want to learn more about the strategies and tools of green chemistry and how they might be applying in the academic lab setting, you can learn more by consulting the references and the resources listed below.

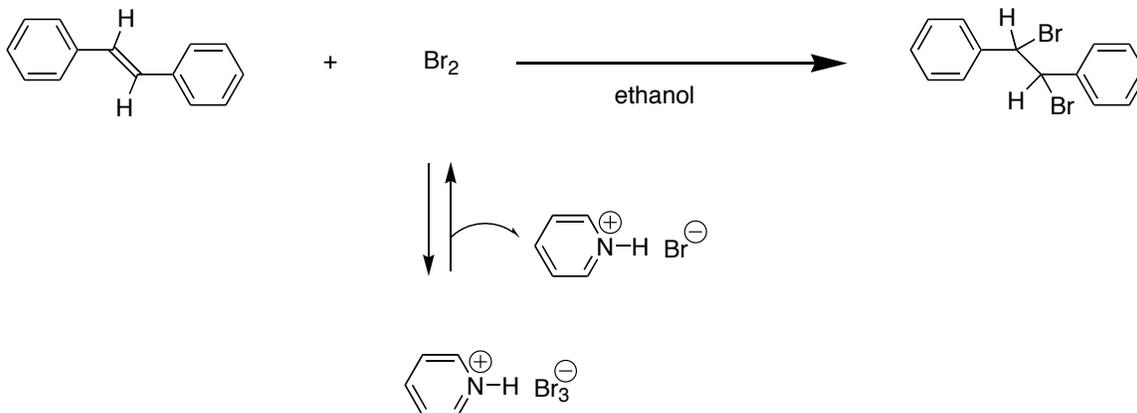
Resources

1. Doxsee, K. M.; Hutchison, J. E. *Green Organic Chemistry: Strategies, Tools and Laboratory Experiments*, First Edition, Brooks/Cole, 2004. pp. 244. Contains ten chapters of background on green chemistry and 19 original laboratory experiments.
2. *Greener Approaches to Undergraduate Chemistry Experiments*, American Chemical Society, 2002, Kirchhoff, M.; Ryan, M. A., Eds.
3. Parent, K. E.; Kirchhoff, M., Eds. *Going Green: Integrating Green Chemistry into the Curriculum*; American Chemical Society: Washington, DC, 2004.
4. Greener Educational Materials (GEMs) for Chemists Database at the University of Oregon: <http://www.uoregon.edu/~greenlab/>
5. McKenzie, L. C.; Huffman, L. M.; Parent, K. E.; Thompson, J.; Hutchison, J. E. "Patterning Self-assembled Monolayers on Gold: Green Materials Chemistry in the Teaching Laboratory," *J. Chem. Ed.* **2004**, *81*, 545-548.
6. McKenzie, L. C.; Thompson, J. E.; Sullivan, R.; Hutchison, J. E. "Green chemical processing in the teaching laboratory: A convenient liquid CO₂ extraction of natural products," *Green Chem.* **2004**, 355-358.
7. McKenzie, L. C.; Huffman, L. M.; Hutchison, J. E. "The Evolution of a Green Chemistry Laboratory Experiment: Greener Brominations of Stilbene," *J. Chem. Educ.* **2004**, *In press*.

Appendix:

GREEN ORGANIC LABORATORY EXPERIMENTS GRAPHICAL TABLE OF CONTENTS – From Reference 1

1. BROMINATION OF AN ALKENE: PREPARATION OF STILBENE DIBROMIDE (P. 114-118)

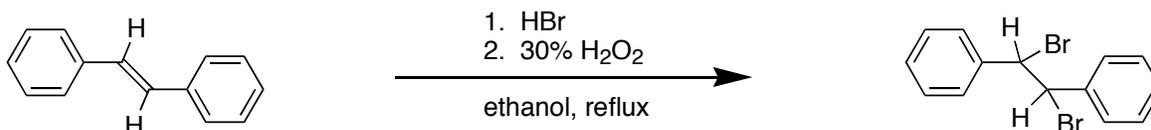


Concepts/techniques: Reactivity of alkenes with halogens, reaction setup, vacuum filtration, melting point determination, recrystallization.

Green chemistry messages: Use of a more benign solvent (substitution of ethanol for chlorinated solvents) and a more benign reagent, pyridinium tribromide.

Experiment development notes: We developed this experiment based upon some leads from Wilcox and Wilcox (Experimental Organic Chemistry, Prentice Hall, 1995) and the original report of the tribromide reagent by Djerassi and Scholz (*J. Am. Chem. Soc.* **1948**, *70*, 417). We made the reaction greener by substituting ethanol for acetic acid as the reaction solvent, in addition to substituting pyridinium hydrobromide perbromide for liquid bromine.

2. A GREENER BROMINATION OF STILBENE (P.119-122)

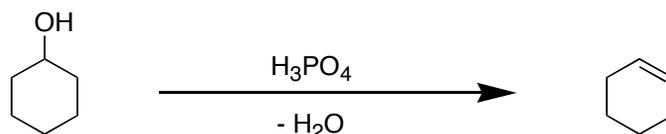


Concepts/techniques: Same as above.

Green chemistry messages: Greener reagents. Improved atom economy.

Experiment development notes: We developed this experiment to improve upon the pyridinium tribromide approach. The initial suggestion for the route was made by Dieter Lenoir. Conditions were adapted by Lauren Huffman from "Synthetic Methods and Reactions; 39. Phase Transfer Catalyst Promoted Halogenation of Alkenes with Hydrohalic Acid/Hydrogen Peroxide," Ho, T. -L.; Gupta, B.G.B.; Olah, G.A. *Synthesis*, **1977**, *10*, 676-677, and "On Oxyhalogenation, Acids, and non-mimics of bromoperoxidase enzymes," Rothenberg & Clark, *Green Chemistry* **2000**, *2*, 248-251.

3. PREPARATION AND DISTILLATION OF CYCLOHEXENE (P.123-127)

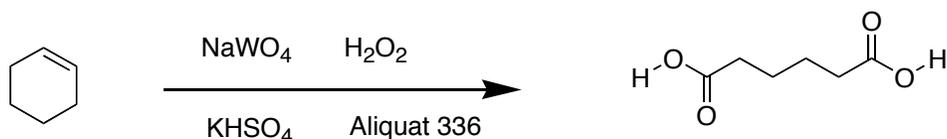


Concepts/techniques: Preparation of an alkene by alcohol dehydration, liquid-liquid extraction, distillation, boiling point determination, IR spectroscopy.

Green chemistry messages: No added solvent, use of a less hazardous and more effective reaction (H_3PO_4 instead of H_2SO_4). The product from this experiment is recycled as the starting material for the adipic acid.

Experiment development notes: This experiment is in most (all) organic lab texts in various forms. Some use sulfuric acid as a catalyst whereas others use phosphoric acid. We use phosphoric acid as a greener reagent.

4. SYNTHESIS AND RECRYSTALLIZATION OF ADIPIC ACID (P. 128-132)

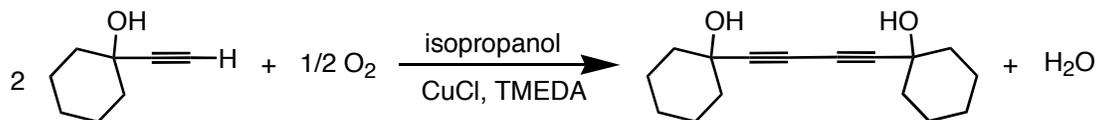


Concepts/techniques: Reactivity of alkenes, recrystallization, melting point determination, polymer chemistry, catalysis, phase transfer catalysis. Oxidative cleavage of a double bond produces a dicarboxylic acid, adipic acid, which is an important precursor to the polymer Nylon 6,6.

Green chemistry messages: Greener oxidizing agent, avoids the use of solvent by using the phase transfer catalyst. Cyclohexene made in a previous lab is used (recycled) as the starting material. It is possible to reuse the aqueous layer containing the tungstate catalyst a number of times.

Experiment development notes: We developed this experiment from the recent (September 11, 1998) primary literature (*Science* **1998**, 281, 1646-1647 "A 'Green' Route to Adipic Acid: Direct Oxidation of Cyclohexenes with 30 Percent Hydrogen Peroxide"). Scott Reed made a number of important modifications to the procedure including decreasing the reaction time from about 24 hours to 3 hours and discovering an in situ method for generating the phase transfer catalyst.

5. OXIDATIVE COUPLING OF ALKYNES: THE GLASER- EGLINTON-HAY COUPLING (P. 133-140)

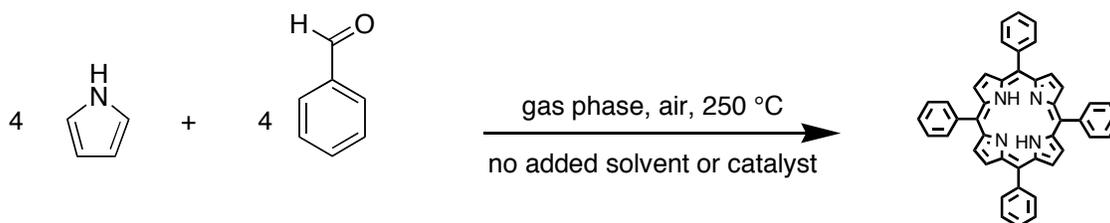


Concepts/techniques: Reactivity of alkynes. Formation of carbon-carbon bonds through oxidative coupling. Standard laboratory skills, use of decolorizing carbon as an aid to purifying crude solids by recrystallization, thin-layer chromatography, and IR spectroscopy of a solid.

Green chemistry messages: Use of a catalyst to direct the course of the reaction, use of oxygen in air as the oxidant in the transformation. A more benign solvent is being used.

Experiment development notes: This experiment was patterned after the same transformation in Wilcox and Wilcox (Experimental Organic Chemistry, Prentice Hall, 1995) and Zanger and McKee (Small Scale Synthesis: A Laboratory Textbook of Organic Chemistry, W.C. Brown Co. 1995). We modified the procedures, including changing the solvent (so that the experiment worked reliably in our students hands) and added TLC training to the experiment.

6. GAS PHASE SYNTHESIS AND VISIBLE SPECTROSCOPY OF AN AROMATIC COMPOUND: SYNTHESIS OF 5,10,15,20-TETRAPHENYLPORPHYRIN (P. 141-146)

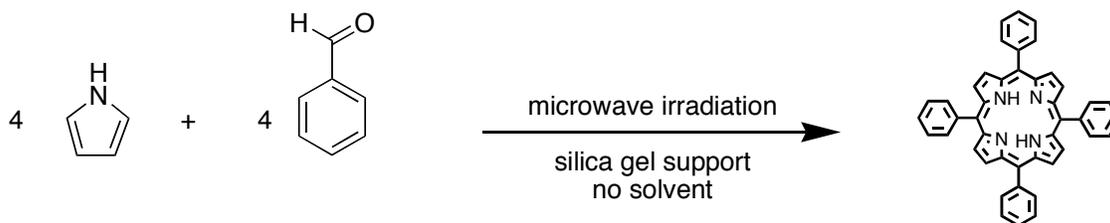


Concepts/techniques: Electrophilic aromatic substitution, synthesis of a complex molecule, gas phase reactions, column chromatography (which is made easier in this case because of the intense (and beautiful) colors of the porphyrin product and the impurities), UV/visible spectroscopy, and TLC.

Green chemistry messages: This gas phase conditions eliminate hazardous solvents in the preparation of organic compounds and provides additional examples of how corrosive reagents can be avoided and air can be used as an oxidant.

Experiment development notes: This is another experiment taken from the recent primary literature ("Synthesis of *meso* substituted porphyrins in air without solvents or catalysts," *Chem. Commun.* **1997**, 2117-2118). Very few details were given in the original report. Marvin Warner put considerable time into developing/optimizing the method so that it will work reliably in the teaching laboratory. This is a great experiment that involves gas-phase synthesis of a complex molecule followed by visually appealing column chromatography.

7. MICROWAVE SYNTHESIS OF TETRAPHENYLPORPHYRIN (P. 147-154)

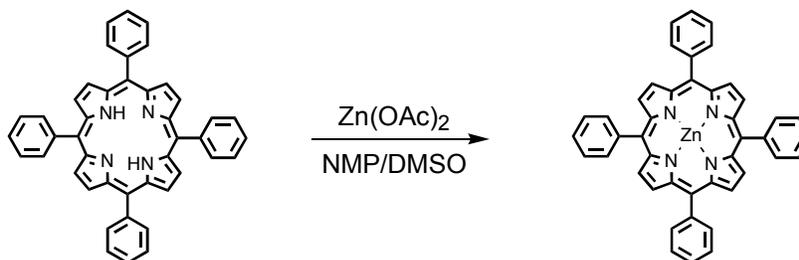


Concepts/techniques: Electrophilic aromatic substitution, synthesis of a complex molecule, microwave-induced reactions, column chromatography (which is made easier in this case because of the intense (and beautiful) colors of the porphyrin product and the impurities), UV/visible spectroscopy, and TLC

Green chemistry messages: Solventless, solid-supported synthesis; microwave heating of reaction mixtures; more benign solvent systems for chromatography

Experiment development notes: This experiment was developed at the University of Oregon based upon the original report from Petit *et al.* (Petit, A.; Loupy, A.; Maillard, P.; Momenteau, M. *Synth. Commun.* **1992**, 22, 1137). Jim Hutchison, Marvin Warner and Gary Succaw adapted this procedure for use in our organic teaching labs.

8. METALLATION OF TETRAPHENYLPORPHYRIN (P. 155-159)



Concepts/techniques: Coordination chemistry, visible spectroscopy

Green chemistry messages: More benign solvents

Experiment development notes: The conditions for this metallation reaction were developed by Marvin Warner.

9. MEASURING SOLVENT EFFECTS: KINETICS OF HYDROLYSIS OF TERT-BUTYL CHLORIDE (P. 160-165)

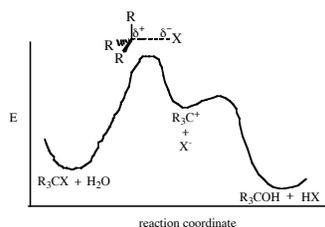


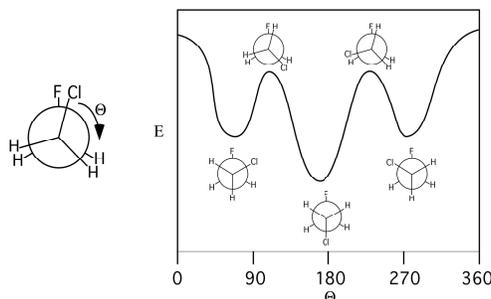
Fig. 1

Concepts/techniques: Solvent effects on the rates of a reactions, chemical kinetics, acid-base titrations. A common strategy in reducing or eliminating hazards in a synthesis involves replacing a hazardous solvent with a more benign one. This experiment illustrates how a solvent change may also influence the rate or course of the reaction.

Green chemistry messages: The important green chemistry concept emphasized in this experiment is that the nature of the solvent can have dramatic effects on reaction rates.

Experiment development notes: The effects of solvent on reaction rate using a classic kinetics experiment that has been reported in numerous texts. We have expanded the range of solvents used and made the experiment a cooperative investigation where pairs of students each investigate a different solvent and share their results with the rest of the class.

10. MOLECULAR MECHANICS MODELING (P. 166-172)

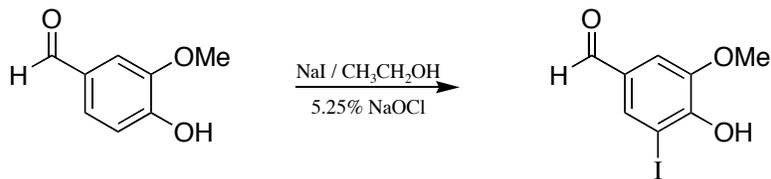


Concepts/techniques: Molecular mechanics modeling, chemical structure. MM computational methods allow us to explore molecular structure and conformation of a variety of organic compounds.

Green chemistry messages: Computer modeling is a useful tool in green chemistry because it allows you to design products and plan syntheses so that you have a better chance of making a compound with the desired properties without having to screen (synthesize and study) many compounds. In this way, computer modeling reduces chemical exposure for the chemist and eliminates the waste / emissions.

Experiment development notes: This module was developed from scratch at the Univ. of Oregon by Jim Hutchison and Marvin Warner.

11. ELECTROPHILIC AROMATIC IODINATION OF 4'-HYDROXYACETOPHENONE OR VANILLIN WITH BLEACH AND NAI (P. 173-179)

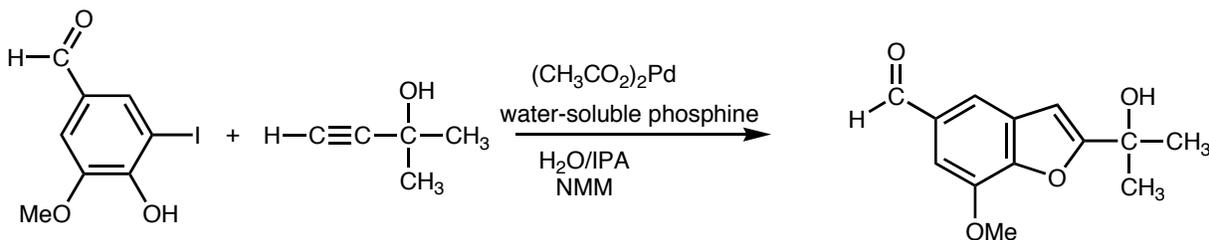


Concepts/techniques: Electrophilic aromatic substitution, recrystallization, melting point determination

Green chemistry messages: Safer and easier to handle reagents and solvents, more selective reagents, greener reagents and solvents

Experiment development notes: The procedure for this iodination was originally adapted from Edgar, K.J.; Falling, S.N. *J. Org. Chem.* **1990**, *55*, 5287-5291 for use for 4'-hydroxyacetophenone by Robert Gilbertson. Adaptation of the procedure for use with vanillin was done by Gary Succaw, Lauren Huffman and Lallie McKenzie.

12. NATURAL PRODUCT SYNTHESIS - PALLADIUM-CATALYZED ALKYNE COUPLING/INTRAMOLECULAR ALKYNE ADDITION (P. 180-186)

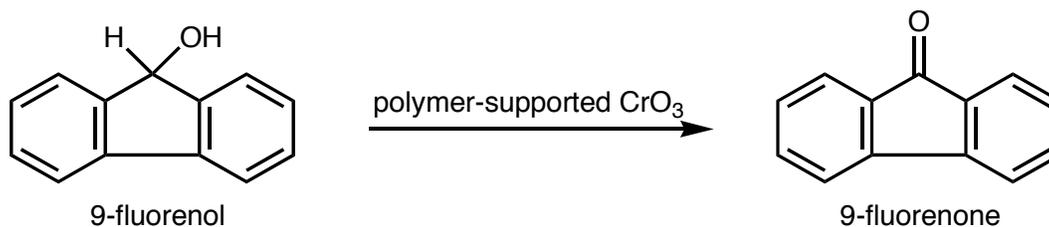


Concepts/techniques: Alkyne chemistry (acetylides, addition reactions), substitution reactions, organometallic chemistry, air-sensitive compounds and techniques for handling them, natural product synthesis

Green chemistry messages: Aqueous organometallic chemistry, catalysis, efficient synthetic routes

Experiment development notes: We developed this experiment based upon the original report from Amatore *et al.* (*J. Org. Chem.* **1995**, *60*, 6829). Ken Doxsee and Gary Succaw adapted this procedure for initial use in our organic teaching labs. In its initial form, the procedure was carried out in aqueous dimethylformamide and the product of the reaction was a liquid. Robert Gilbertson found conditions where the reaction could be carried out in water with a little added NMP and a solid product could be obtained. Subsequent optimization of the procedure and extension of the method for use with 5-iodovanillin was carried out by Gary Succaw and Lauren Huffman.

13. RESIN-BASED OXIDATION CHEMISTRY (P. 187-195)

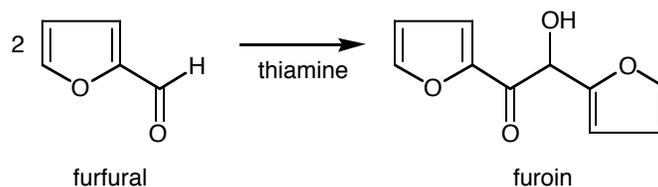


Concepts/techniques: Oxidation chemistry, polymer-supported reagents

Green chemistry messages: Nontraditional reagents and conditions, recyclable reagents, separations facilitated by polymer-supported reagents

Experiment development notes: This experiment was originally reported by Wade and Stell ("A laboratory introduction to polymeric reagents," *J. Chem. Ed.* **1980**, 57, 438.) and was adapted for use in our labs by Ken Doxsee.

14. CARBONYL CHEMISTRY: THIAMINE-MEDIATED BENZOIN CONDENSATION OF FURFURAL (P. 196-201)

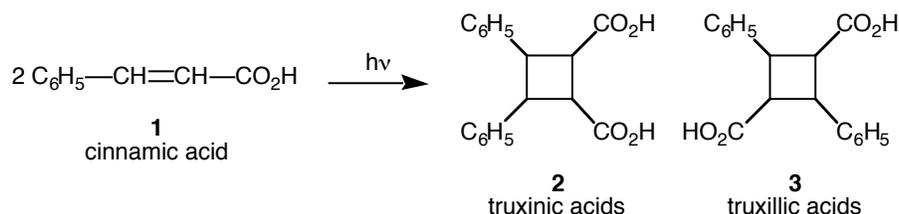


Concepts/techniques: Reactions of carbonyl compounds; oxidation chemistry; carbon skeleton rearrangements

Green chemistry messages: Safer and easier to handle reagents and solvents

Experiment development notes: This version of the benzoin condensation is catalyzed by thiamine (Vitamin B₁) rather than cyanide and uses furfural in place of benzaldehyde as the substrate. The procedure was adapted from the original reports by Breslow ("On the Mechanism of Thiamine Action. IV. Evidence from Studies on Model Systems," *J. Am. Chem. Soc.* **1958**, 80, 3719), Lee et al. ("Benzoin condensation reactions of 5-membered heterocyclic compounds," *J. Heterocyclic Chem.* **1992**, 29, 149) and Hanson ("The preparation of furoin-a biomimetic reaction," *J. Chem. Educ.* **1993**, 70, 257) by Ken Doxsee.

15. SOLID-STATE PHOTOCHEMISTRY (P. 202-213)

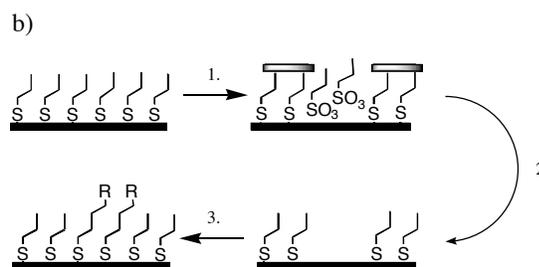


Concepts/techniques: Photochemistry, crystal engineering, identification of unknowns, recrystallization

Green chemistry messages: Photochemical methods, solid-state reactions, control of product distribution by templating

Experiment development notes: This experiment is included in several of the traditional organic laboratory texts and was adapted for our use by Ken Doxsee.

16. APPLICATIONS OF ORGANIC CHEMISTRY – PATTERNING SURFACES WITH SELF-ASSEMBLED MOLECULAR FILMS (P. 214-225)

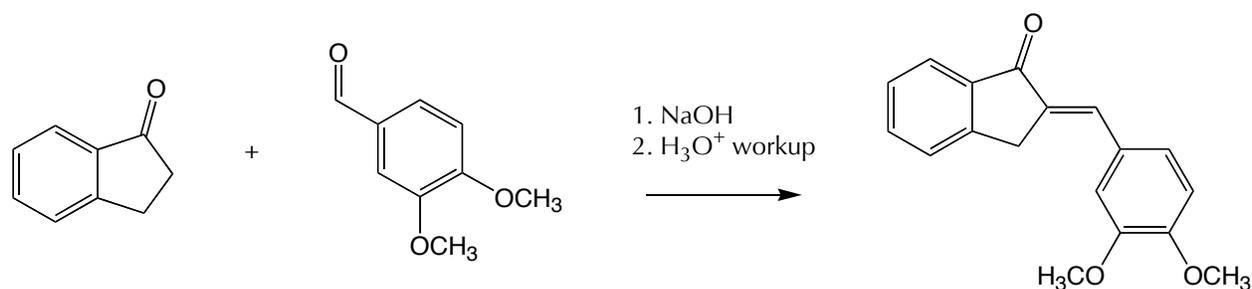


Concepts/techniques: Organic materials chemistry, introduction to surface chemistry, self-assembled monolayers (SAMs), controlling surface properties with organic thin films; microcontact printing

Green chemistry messages: Dematerialization, self-assembly under mild conditions. Use of molecular assembly to fabricate complex materials, replacement of polymeric films with molecular layers.

Experiment development notes: This is an original experiment developed at the University of Oregon. Jim Hutchison, Rob Gilbertson and Kathryn Parent developed the initial procedure for use in our organic teaching labs. The procedures for using gold on vinyl substrates were developed by Lallie McKenzie in collaboration with Kathryn Parent. Subsequent optimization of the patterning techniques was carried out by Lallie McKenzie and Lauren Huffman.

17. SOLVENTLESS REACTIONS BETWEEN SOLIDS: AN ALDOL CONDENSATION AND MELTING POINT LAB (P. 226-229)

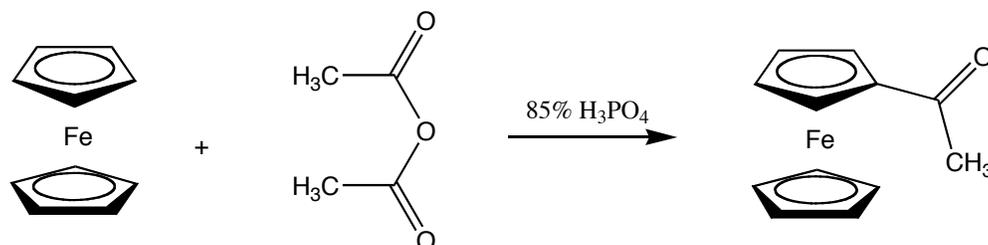


Concepts/techniques: Melting points of solids and mixtures, eutectic mixtures, carbonyl chemistry, the aldol reaction, recrystallization

Green chemistry messages: Solventless reactions between solids, atom economy

Experiment development notes: This experiment was adapted by Lauren Huffman from the primary literature reported by Scott et al. ("Understanding Solid/Solid Organic Reactions," *J. Am. Chem. Soc.* **2001**, *123*, 8701-8708).

18. ACETYLATION OF FERROCENE (P. 230-233)

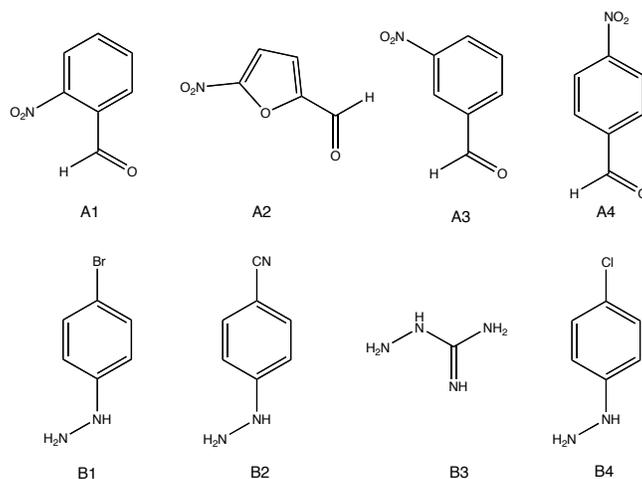


Concepts/techniques: Electrophilic aromatic substitution, recrystallization, thin-layer chromatography

Green chemistry messages: Use of a more benign reagent. Friedel-Crafts acylation usually requires the use of a strong Lewis acid, typically aluminum trichloride, as a catalyst. Ferrocene's higher reactivity permits the use of a more benign catalyst – phosphoric acid.

Experiment development notes: This procedure was adapted from the classic procedure in Feiser and Williamson by Lallie McKenzie.

19. COMBINATORIAL CHEMISTRY/ANTIBIOTIC SCREENING EXPERIMENT (P. 234-244)



Concepts/techniques: Combinatorial chemistry, carbonyl chemistry, screening assays for active compounds

Green chemistry messages: Waste minimization. The use of combinatorial chemistry to discover new compounds using highly parallel techniques, on a small scale, without the need for isolation and purification of the individual compounds offers a number of advantages for waste minimization.

Experiment development notes: These procedures were adapted from "Combinatorial Synthesis and Discovery of an Antibiotic Compound: An Experiment Suitable for High School and Undergraduate Laboratories," by Wolkenberg, S.E. and Su, A.I., *J. Chem. Ed.* **2001**, 78, 784.